



Review Article

ISSN : 2277-3657
CODEN(USA) : IJPRPM

Lovastatin Use in Transplant: A Review and Survey

Abigail Owusu¹, Kany Bonnaire¹, Bisrat Hailemeskel^{2*}

¹Clinical & Administrative Pharmacy Sciences, College of Pharmacy, Howard University, Washington, DC 20059, USA.

²College of Pharmacy, Howard University, Washington, DC 20059 US, USA.

*Email: bhailemeskel@howard.edu

ABSTRACT

Despite advancements in cardiac transplant therapies, rejection remains a significant issue. Lovastatin, a statin drug with promising immunomodulatory effects, has garnered attention as a potential treatment for heart transplant rejection. Studies collectively highlight the ability of lovastatin to influence T-cell activation, reduce episodes of acute rejection, and maintain graft function. These findings offer promising avenues for enhancing transplant success rates and patient outcomes with the use of lovastatin. This survey aimed to explore perceptions of the use of lovastatin in the management of post-cardiac transplant rejection. Participants with diverse backgrounds were surveyed about their candidacy for lovastatin, perceived risks of non-approved drugs, and dyslipidemia prophylaxis importance. Analysis of 39 respondents revealed demographic trends, predominantly female (59%) and aged 18-24 years (82.1%), primarily from Maryland and Virginia. Most were already employed, many in pharmacy-related roles, and had a 4-year degree as their highest level of education. While 70.3% recognized lovastatin as a statin, opinions on its efficacy varied. Notably, 51.4% believed it should be considered for the management of rejection. Demographic comparisons revealed significant differences in opinions, such as age groups differing in lovastatin's suitability ($P = 0.003$) and awareness of unapproved medications ($P < 0.001$). This study highlights the diverse views on the effectiveness of lovastatin for heart transplant rejection and emphasizes the need for further investigation. Patient education and prevention of dyslipidemia are essential for transplant survival. Given the array of viewpoints, further research is warranted to clarify the safety and effectiveness of lovastatin in this context.

Keywords: Lovastatin, Transplant, Pharmacy, Students, Survey, Opinion

INTRODUCTION

One of the greatest discoveries in medicine is organ transplantation, which gives patients with end-stage organ failure hope and a longer life expectancy. However, the success of organ transplantation is often hindered by complications arising from immunosuppressive therapy, primarily aimed at preventing graft rejection. These side effects, which include metabolic abnormalities, infections, and cardiovascular events, all add to patient morbidity and transplant rejection [1].

Lovastatin belongs to the statin drug class, which is commonly prescribed to treat hyperlipidemia and prevent cardiovascular disease (CVD). The rate-limiting enzyme in the manufacture of cholesterol, 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase, is competitively inhibited by lovastatin. Lovastatin lowers circulation levels of low-density lipoprotein cholesterol (LDL-C) and consequently the risk of atherosclerosis and cardiovascular events by blocking the liver's ability to synthesize cholesterol [2].

Lovastatin is effective in lowering LDL-C levels in a range of patient demographics. When taken as prescribed, lovastatin can lower LDL-C levels by roughly 24-40%, according to randomized controlled trials (RCTs).

Moreover, lovastatin has been demonstrated to enhance triglycerides, high-density lipoprotein cholesterol, and total cholesterol (HDL-C). Studies with extended follow-up have shown that lovastatin medication continues to lower the risk of cardiovascular events and death [3].

Lovastatin has a good safety profile and is generally well tolerated. But lovastatin, like other statins, has some side effects, the most prominent of which are hepatotoxicity, myopathy, and gastrointestinal problems. Adverse effect risk is dose-dependent and may be impacted by age, co-occurring medical conditions, and concurrent medication use. The most dangerous side effect of lovastatin is myopathy, which manifests as muscle soreness, weakness, or tenderness and necessitates immediate medical attention. Even though it is uncommon, hepatotoxicity can cause severe cases of hepatocellular injury or increased liver enzymes. The majority of the time, minor and temporary gastrointestinal side effects include nausea, abdominal pain, and diarrhea.

Lovastatin in transplant – Review of studies

A study was conducted in Sana'a, Yemen which aimed to look at aspects such as attitudes and perceptions towards the initiation of statin drugs in preventing CVD. 428 healthcare workers, including physicians and pharmacists, who worked in a range of healthcare facilities, such as public and private hospitals, private clinics, and neighborhood pharmacies, provided data for the study. The following sections made up the questionnaire: demographic data, clinical knowledge of statin medication, monitoring parameter comprehension, and judgments of obstacles to the application of guidelines. Despite the fact statins are widely used in modern clinical practice, the study revealed significant knowledge gaps among participants. Notably, a significant number of healthcare professionals were unable to determine which patient groups required an assessment of their risk for atherosclerotic cardiovascular disease (ASCVD) before starting statin therapy; almost 80.4% were unable to make this crucial determination. Moreover, a clear gap in understanding was observed concerning the definitions of statin strength, the ideal timing of administration, and contraindications. More specifically, several respondents showed a lack of knowledge on the ideal timing for taking statins, the suggested dose intensities for various patient cohorts, and the situations when taking statins should not be done, such as when a woman is pregnant or nursing. These findings highlight a pressing need for targeted educational interventions and comprehensive training programs aimed at enhancing healthcare workers' knowledge [4].

The goal of this study is to evaluate the literature on the perspectives on lovastatin use in cardiac transplant settings. It also investigates the knowledge and opinions of survey participants on the topics. Demographic characteristics such as age, gender, residence state, type of work, years worked, and highest education attended will be considered through survey-based research methodologies to see how these aspects affect people's attitudes and comprehension of lovastatin therapy. This part of the study looks for misconceptions or knowledge gaps about lovastatin use among those involved in heart transplantation.

MATERIALS AND METHODS

The survey was done as a part of the Drug Information, a 2-credit hour mandatory course for incoming pharmacy students at Howard University, College of Pharmacy. Participants completed a structured questionnaire that included questions about their age, gender, state of residence, employment history, income, and educational attainment.

Knowledge-based questions were incorporated into the questionnaire to gauge the participants' comprehension of lovastatin and its significance in managing dyslipidemia following heart transplantation. Opinion-based questions were also added to get viewpoints on FDA approval, patient awareness of non-approved medications, and the suitability of lovastatin for treating rejection from heart transplants.

Statistical methods such as Pearson correlation and chi-square tests were used to analyze the data and look for relationships between opinions on lovastatin and demographic factors. Comparative research was carried out utilizing demographic characteristics to detect any relationships with opinions regarding the use of lovastatin.

RESULTS AND DISCUSSION

A total of 39 participants completed the survey (**Table 1**). The majority of them were female participants, who constituted 59.0% of the responses. Regarding age demographics, a significant portion of the respondents, 82.1%, were young adults aged 18 to 24 years. Geographically, responses were widespread, with the highest

representation from Maryland (25.6%), followed by Virginia (17.9%) and Washington, DC (5.1%), yet a considerable 51.3% of participants hailed from other states, indicating the survey's broad geographic appeal.

Table 1. Demographic (age, gender, states; N = 39)

Demographic	Frequency	Percent
Gender		
Male	16	41.0%
Female	23	59.0%
Age		
18 - 24	32	82.1%
25-34	0	0%
35 & older	9	17.9%
State		
Washington, DC	2	5.1%
Maryland	10	25.6%
Virginia	7	17.9%
Other states	20	51.3%

The demographic data (**Table 2**) shows that 87.2% had work experience before enrollment in the pharmacy program, with a significant portion (30.8%) earning less than \$10,000 annually. Regarding the type of work, 33.3% were engaged in pharmacy-related jobs, and 30.8% in healthcare but not directly in pharmacy. Work duration varied, with 48.7% reporting 1-3 years of experience. Educational backgrounds were diverse, yet 74.4% had achieved a 4-year degree before joining the program. Notably, missing data impacted income (7.7%), type of work (15.4%), and years worked (10.3%) responses.

Table 2. Demographic (work experience, income, etc.)

Demographic	Frequency	Percent
Have you worked or had a job before coming to Howard University's pharmacy program? N=39		
Yes	34	87.2
No	5	12.8
Annual income from your Job if you have worked (N = 39)		
Less than \$10,000	12	30.8
\$10,000 - \$19,999	2	5.1
\$20,000 - \$29,999	5	12.8
\$30,000 - \$39,999	7	17.9
\$40,000 - \$49,999	4	10.3
Greater than \$49,999	6	15.4
If you worked before coming to HU, what kind of work have you had? (N=39)		
Non-Pharmacy or Non-Health care related	8	20.5
Pharmacy Related	13	33.3
Non-pharmacy but healthcare-related	12	30.8
If you worked before coming to HU, how many years have you worked (in years)? (N = 39)		
< 1 Year	3	7.7
1-3 Years	19	48.7
4-5 years	2	5.1

> 5 years	11	28.2
Highest Education Attended Before Coming To Howard Pharmacy School (N = 39)		
Some college	4	10.3
2-year degree	3	7.7
4-year degree	29	74.4
Professional Degree	3	7.7

Table 3 summarizes responses to knowledge-based questions on medication and treatment protocols, revealing a consensus among participants. Approximately 91.9% agree that lovastatin is classified as a statin, with a notable 70.3% strongly affirming this classification (Question #1). Statins are indeed a group of medications commonly used to lower cholesterol levels in the blood. They work by inhibiting the enzyme HMG-CoA reductase, which plays a central role in the production of cholesterol in the liver. Lovastatin, specifically, is used to reduce the risk of heart disease and improve cholesterol levels by lowering levels of "bad" LDL cholesterol and triglycerides in the blood while raising "good" HDL cholesterol.

When discussing the importance of dyslipidemia prophylaxis for cardiac transplant survival (Question #2), 86.5% of respondents answered it correctly. Furthermore, a substantial 83.8% of participants believe that adhering to statin guidelines, particularly with lovastatin, can enhance survival rates post-cardiac transplant (Question #3). The statement that "Prophylaxis of dyslipidemia seems to be critical for cardiac transplant survival" aligns well with current clinical observations and research. Dyslipidemia is commonly seen in heart transplant recipients, primarily due to immunosuppressive therapy, and is a significant contributor to the development of cardiac allograft vasculopathy (CAV), a leading cause of morbidity and mortality post-transplant. Managing lipid levels in these patients is indeed critical, as dyslipidemia has been linked to accelerated CAV and poor long-term outcomes.

Studies show that CAV affects many transplant recipients, with a noted progression in intimal thickening that can lead to graft failure. This condition manifests differently from typical atherosclerosis, often involving more diffuse and concentric lesions, and is exacerbated by factors like inflammation and immunological responses. Moreover, systemic inflammation, marked by elevated high-sensitivity C-reactive protein levels, is also commonly observed in transplant recipients and correlates with the development of CAV. Managing these inflammatory processes, alongside strict control of lipid levels, forms a cornerstone of post-transplant care to improve survival rates and reduce the incidence of CAV (American College of Cardiology). Thus, it's evident that maintaining optimal lipid levels and managing cardiovascular risk factors is crucial for the longevity and quality of life of heart transplant recipients, underscoring the importance of dyslipidemia prophylaxis in these patients.

Regarding lovastatin's efficacy in treating dyslipidemia, 86.4% acknowledge its effectiveness (Question #4). The evidence from the literature search revealed that there is strong support for the use of statins as a critical component in the post-transplant care regimen to enhance patient outcomes and extend survival. This recommendation is backed by consistent findings across various studies that highlight the protective effects of statins against complications that affect transplant survival.

Lastly, opinions on reducing statin doses for prophylactic purposes are mostly positive, with 86.5% in agreement (Question #5). In cardiac transplant patients, the dose of statins like lovastatin may be reduced to manage dyslipidemia while minimizing the risk of interactions with immunosuppressive medications. These medications, like calcineurin inhibitors, can increase statin levels in the blood, heightening the risk of side effects such as myopathy. The goal is to effectively balance cholesterol management and prevent complications like cardiac allograft vasculopathy while ensuring patient safety. Regular monitoring of lipid levels and statin efficacy is essential in this patient group.

Table 3. Knowledge-based questions

Knowledge-based Questions	Correct Answers	Number (%) of participants with correct answers
1. Lovastatin belongs to a class of drugs called statins	True	34 (91.9%)
1. Prophylaxis of dyslipidemia seems to be critical for cardiac transplant survival.	True	32 (82.0%)

2. Chances of survival are higher if a statin like lovastatin is taken within guidelines after a cardiac transplant.	True	31 (79.4%)
3. Lovastatin is an efficient dyslipidemia drug.	True	32 (82.0%)
4. The dose of statins like lovastatin might be reduced for cardiac transplant when used prophylactically.	True	32 (82.0%)

Table 4 summarizes the results of the opinion-based questions. The responses to statements on the use of lovastatin for managing cardiac transplant rejection show varied opinions (Statement #1). About 70.3% of participants believe lovastatin could be considered for this purpose. In terms of the risks associated with organ rejection and the use of non-approved drugs, 75.7% caution against their use (Statement #2). When it comes to FDA approval for lovastatin, opinions are split; 48.6% agree it should be awaited before use (Statement #4). However, there's substantial support (94.5%) for further FDA research on lovastatin, with almost half strongly agreeing. Moreover, the consensus on the importance of patient awareness about non-approved drugs is high, with 86.5% acknowledging it as crucial (Statement #5). This demonstrates diverse views on lovastatin's role in post-transplant care, highlighting the importance of regulatory approval and patient education.

Table 4. Opinion-based questions

Statements	Strongly Disagree	Somewhat disagree	Somewhat Agree	Strongly Agree	Total
1. I think lovastatin should be a candidate for the management of cardiac transplant rejection since organ rejection is a major issue with current treatment options.	5.4%	24.3%	51.4%	18.9%	100.0%
2. Organ rejection is deadly if it occurs, I do not recommend any non-approved drug.	--	24.3%	24.3%	51.4%	100.0%
3. Lovastatin should be used until it gets FDA approval.	18.9%	32.4%	35.1%	13.5%	100.0%
4. The FDA should proceed with research on lovastatin.	--	5.4%	45.9%	48.6%	100.0%
5. I believe patients should be made aware before using any non-approved drug to treat their illness.	--	13.5%	27.0%	59.5%	100.0%

While lovastatin is effective in managing cholesterol and has shown benefits in reducing the incidence of CA post-transplant, its role specifically in managing transplant rejection isn't directly established. Transplant rejection is primarily managed through immunosuppressive drugs rather than cholesterol-lowering medications. Proposing lovastatin as a direct treatment for transplant rejection would require extensive clinical research focusing on its immunomodulatory effects, if any.

The analysis indicates a favorable view of lovastatin for cardiac transplant management, with 60% of younger adults (18-24 years) somewhat agreeing and 13.3% strongly agreeing on its benefits, while 42.9% of older adults (35 and above) strongly support its consideration.

Concerning the risks of organ rejection and non-approved drugs, 75% of older respondents strongly advise against their use, contrasted with 43.3% of younger individuals. Moreover, there's a high consensus on the importance of patient awareness about non-approved drugs, with 54.8% of younger and 75% of older adults strongly agreeing. Most agree that organ rejection is a serious condition and managing it with non-FDA-approved drugs could pose significant risks. The use of approved and well-researched immunosuppressants is critical to ensure the safety and efficacy of treatment in transplant patients.

Lovastatin is already FDA-approved for managing cholesterol levels but not specifically for preventing transplant rejection. It should only be used within its approved indications unless further research supports new applications and subsequent FDA approval is granted for those uses.

Regarding lovastatin's usage and FDA approval, opinions varied significantly based on respondents' work backgrounds. Those in non-pharmacy or healthcare-related fields showed divided views, with 25% somewhat agreeing and another 25% somewhat disagreeing that lovastatin should await FDA approval. Pharmacy-related

workers predominantly somewhat disagreed (58.3%), indicating a cautious stance towards its usage without FDA endorsement. However, the majority from both pharmacy-related (50%) and non-pharmacy healthcare-related (87.5%) fields supported further FDA research on lovastatin. An agreement that lovastatin belongs to the statin class was unanimous in non-pharmacy healthcare-related fields. Views on dyslipidemia prophylaxis and statin dose reduction for cardiac transplant also varied, with significant disagreement on dose reduction from pharmacy-related respondents (66.7%) and non-pharmacy but healthcare-related fields (72.7%). This illustrates diverse perspectives influenced by professional experience, with a consensus on the need for lovastatin research and acknowledgment of its statin classification.

The data in **Table 5** shows varied views on lovastatin and dyslipidemia prophylaxis based on professional background: 50% of non-pharmacy/non-healthcare respondents strongly disagreed with lovastatin usage, while 27.3% from non-pharmacy but healthcare fields strongly agreed. For dyslipidemia prophylaxis, 75% of pharmacy-related fields strongly agreed on its importance. Skepticism towards lovastatin was highest among non-pharmacy/non-healthcare fields (58.3% somewhat disagreed), indicating significant differences in opinions tied to respondents' work experience, as evidenced by p-values of .042 and .045, highlighting the influence of professional background on attitudes toward medical treatments.

The table details how work experience influences opinions on lovastatin for cardiac transplant rejection management and the role of dyslipidemia prophylaxis in transplant survival among Howard University newcomers. It reveals a clear trend: those with over 5 years of work experience are the most likely to strongly disagree (100%) with lovastatin's suitability for cardiac transplant rejection, but they also strongly agree (40-50%) on the critical importance of dyslipidemia prophylaxis for survival, indicating a nuanced understanding of treatment complexities. In contrast, respondents with 1-3 years of work experience predominantly somewhat disagree with lovastatin's suitability (60%) yet constitute the majority that somewhat agree on its potential benefits (83.3%) and the necessity of dyslipidemia prophylaxis (55.6%). These insights suggest that longer work experience correlates with a stronger emphasis on prophylaxis and a cautious approach to unapproved drugs like lovastatin, whereas those with lesser experience are more open to considering its benefits.

The table also summarizes opinions on the use of non-approved drugs for organ rejection, revealing broad consensus across educational backgrounds, with a significant lean towards caution. A mere 6.1% of all respondents strongly disagreed with the statement, emphasizing the general apprehension towards non-approved medications. The most common stance was strong agreement on the dangers of organ rejection and avoiding non-approved drugs, held by 72.7% of participants, notably with those holding professional degrees (42.4%) showing the highest concurrence. Somewhat disagreeing (39.4%) and somewhat agreeing (36.4%) perspectives also highlight varied levels of concern, especially among those with a 4-year degree, indicating a widespread acknowledgment of the risks associated with organ rejection and the critical evaluation of drug approval status.

The data analyzes attitudes towards lovastatin intake according to guidelines for post-cardiac transplant across different age groups. Key findings show minimal strong disagreement with its use, mainly among those 35 and older. The younger cohort (18-24 years) showed significant consensus towards the benefits, with 18 somewhat agreeing and 9 strongly agreeing on lovastatin's positive impact on survival post-transplant. Overall, the younger age group demonstrates a more favorable outlook towards adhering to statin guidelines after cardiac transplants, reflecting a general optimism about lovastatin's role in enhancing patient outcomes. The table also presents respondents' opinions on various statements related to lovastatin usage and cardiac transplant survival, categorized by their prior work experience, particularly in pharmacy or healthcare-related fields.

Additionally, the data shown illustrates regional attitudes towards the severity of organ rejection and the use of non-approved drugs, revealing a consensus on the risks associated with organ rejection. In Washington, DC, opinions were split evenly between somewhat and strongly agreeing on the statement's severity. Maryland showed a strong concurrence, with 77.8% strongly agreeing. Virginia had the highest rate of strong agreement at 85.7%, indicating widespread caution in the region. Other states displayed a broader range of opinions, with notable percentages both somewhat disagreeing and agreeing. Across all regions, the tendency leans towards recognizing the serious implications of organ rejection and exercising caution against non-approved drugs, albeit with slight regional differences in the level of agreement.

There is a correlation between respondents' work experience before joining the pharmacy program and their views on dyslipidemia prophylaxis in cardiac transplant survival. Those with 1-3 years of work experience are the most likely (54.5%) to recognize its importance, followed by respondents with over 5 years of experience (30.3%). Individuals with less than a year and those with 4-5 years of experience contribute smaller percentages (9.1% and 6.1%, respectively) to the total acknowledgment of dyslipidemia prophylaxis's role. This indicates a broad

recognition of the critical need for dyslipidemia management in cardiac transplant outcomes, varying with the amount of prior work experience.

Table 5. Comparative analysis based on demographic factors ($P < 0.05$)

Demographic Factors	Knowledge or Opinion Questions
Age	*I think lovastatin should be a candidate for the management of cardiac transplant rejection since organ rejection is a major issue with current treatment options
	*Organ rejection is deadly if it occurs, I do not recommend any non-approved drug
	*I believe patients should be made aware before using any non-approved drug to treat their illness
	*Chances of survival are higher if a statin like lovastatin is taken within guidelines after a cardiac transplant
	* Chances of survival are higher if a statin like lovastatin is taken within guidelines after a cardiac transplant.
Residence State	*Organ rejection is deadly if it occurs, I do not recommend any non-approved drug.
	* Organ rejection is deadly if it occurs, I do not recommend any non-approved drug.
	* Organ rejection is deadly if it occurs, I do not recommend any non-approved drug.
Type of work	* Lovastatin should be used until it gets FDA approval.
	* Prophylaxis of dyslipidemia seems to be critical for cardiac transplant survival.
	* Lovastatin should be used until it gets FDA approval.
	* FDA should proceed with research with lovastatin.
	* Prophylaxis of dyslipidemia seems to be critical for cardiac transplant survival.
	* The dose of statins like lovastatin might be reduced for cardiac transplant when used prophylactically.
	* Prophylaxis of dyslipidemia seems to be critical for cardiac transplant survival.
	* Lovastatin belongs to a class of drugs called statins.
Years Worked	* Lovastatin is an efficient dyslipidemia drug.
	* Prophylaxis of dyslipidemia seems to be critical for cardiac transplant survival.
	* I think lovastatin should be a candidate for the management of cardiac transplant rejection since organ rejection is a major issue with current treatment options.
Highest education attended	* Organ rejection is deadly if it occurs, I do not recommend any non-approved drug.

Survey limitations

The primary limitation of this study is the small sample size and the fact that it only addressed pharmacy students at a single university. Additionally, accuracy and response bias are potential risks associated with self-reported data, especially when it comes to sensitive variables like demographic data such as work experience and income. Finally, the result interpretability is restricted by selection bias only including participants attending a specific course. Lack of contextual data about the experiences or backgrounds of the respondents.

CONCLUSION

This survey presents a range of viewpoints regarding the possible application of lovastatin in the treatment of heart transplant rejection. Opinions differ according to age, professional background, and geographic area, even if many people are in favor of its consideration. There is general agreement regarding the significance of patient education and dyslipidemia prophylaxis, regardless of disagreements. To improve patient outcomes in transplant medicine, more research is required to address these divergent perspectives and elucidate the function of lovastatin in transplant therapy.

ACKNOWLEDGMENTS: None

CONFLICT OF INTEREST: None

FINANCIAL SUPPORT: None

ETHICS STATEMENT: None

REFERENCES

1. Kasiske BL, Zeier MG, Chapman JR, Craig JC, Ekberg H, Garvey CA, et al. KDIGO clinical practice guideline for the care of kidney transplant recipients: A summary. *Kidney Int.* 2010;77(4):299-311. doi:10.1038/ki.2009.377
2. Duong H, Bajaj T. Lovastatin. [Updated 2023 Mar 20]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024.
3. Bradford RH, Shear CL, Chremos AN, Dujovne CA, Franklin FA, Grillo RB, et al. Expanded clinical evaluation of lovastatin (EXCEL) study results: Two-year efficacy and safety follow-up. *Am J Cardiol.* 1994;74(7):667-73. doi:10.1016/0002-9149(94)90307-7
4. Al-Ashwal FY, Sulaiman SAS, Sheikh Ghadzi SM, Kubas MA, Halboup A. Physicians and pharmacists' clinical knowledge of statin therapy and monitoring parameters, and the barriers to guideline implementation in clinical practice. *PLoS One.* 2023;18(1):e0280432. doi:10.1371/journal.pone.0280432